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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/776,450	02/11/2004	Wesley K.M. Chong	PC19074	3704
28940	7590 11/29/2004		EXAMINER	
AGOURON PHARMACEUTICALS, INC.			LEE, SUSANNAH E	
10350 NORT LA JOLLA,	H TORREY PINES RO	AD	ART UNIT	PAPER NUMBER
LA JOELA,	SR 72031		1626	
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DATE MAILED: 11/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

	Application No.	Applicant(s)				
	10/776,450	CHONG ET AL.				
Office Action Summary	Examiner	Art Unit				
	Susannah Lee	1626				
The MAILING DATE of this communication appears on the cover sheet with the correspondence address Period for Reply						
A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION. - Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication. - If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely. - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication. - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).						
Status						
1) Responsive to communication(s) filed on						
2a) This action is FINAL . 2b) ☑ This action is non-final.						
3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11, 453 O.G. 213.						
Disposition of Claims						
4)⊠ Claim(s) <u>1-9</u> is/are pending in the application.						
4a) Of the above claim(s) is/are withdrawn from consideration.						
5) Claim(s) is/are allowed.						
6)⊠ Claim(s) <u>1-9</u> is/are rejected.						
7) Claim(s) is/are objected to						
8) Claim(s) <u>1-9</u> are subject to restriction and/or ele	ection requirement.					
Application Papers						
9)☐ The specification is objected to by the Examiner.						
10)☐ The drawing(s) filed on is/are: a)☐ accepted or b)☐ objected to by the Examiner.						
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).						
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).						
11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.						
Priority under 35 U.S.C. § 119						
12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).						
a) ☐ All b) ☐ Some * c) ☐ None of:						
1. Certified copies of the priority documents have been received.						
2. Certified copies of the priority documents have been received in Application No.						
3. Copies of the certified copies of the priority documents have been received in this National Stage						
application from the International Bureau (PCT Rule 17.2(a)).						
* See the attached detailed Office action for a list of the certified copies not received.						
Attachment(s)						
1) Notice of References Cited (PTO-892)	4) Interview Summary					
2) Notice of Draftsperson's Patent Drawing Review (PTO-948) 3) Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)		atent Application (PTO-152)				
Paper No(s)/Mail Date	6) Other:					

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DETAILED ACTION

Claims 1-9 are pending in the instant application.

Priority

This application claims the benefit of U.S. Provisional Application 60/447,329 filed on 12 February 2003.

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

- I. Claims 1-6 are drawn to compounds of Formulas I and II, classified in various subclasses of classes 540, 544, 546, 548 or 549.
- II. Claims 7-9 are drawn to methods of use of compounds of Formulas I and II, classified in various subclasses of classes 540, 544, 546, 548, 549 and 514.

Where an election of Groups I is made, an election of a single compound is further required including an exact definition of each substitution on the base molecule (Formula (I)), wherein a single member at each substituent group or moiety is selected. For example, if a base molecule has a substituent group R1, wherein R1 is recited to be any one of H, OH, COOH, aryl, alkoxy, halogen, amino, etc., then applicant must select a single substituent of R1, for example OH or aryl and each subsequent variable position. In the instant case, upon election of a single compound, the Office will review the claims and disclosure to determine the scope of the independent invention encompassing the elected compound (compounds which are so similar thereto as to be within the same inventive concept and reduction to practice). The scope of an independent invention will encompass all compounds within the scope of the claim, which fall into the same class and subclass as the elected compound, but may also include additional compounds, which fall in related subclasses. Examination will then proceed on the elected

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compound AND the entire scope of the invention encompassing the elected compound as defined by common classification. A clear statement of the examined invention, defined by those class(es) and subclass(es) will be set forth in the first action on the merits. Note that the restriction requirement will not be made final until such time as applicant is informed of the full scope of compounds along with (if appropriate) the process of using or making said compound under examination. This will be set forth by reference to specific class(es) and subclass(es) examined. Should applicant traverse on the ground that the compound are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the compound to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other.

All compounds falling outside the class(es) and subclass(es) of the selected compound and any other subclass encompassed by the election above will be directed to nonelected subject matter and will be withdrawn from consideration under 35 U.S.C. 121 and 37 C.F.R. 1.142(b). Applicant may reserve the right to file divisional applications on the remaining subject matter. (The provisions of 35 U.S.C. 121 apply with regard to double patenting covering divisional applications.)

Applicant is reminded that upon cancellation of claims to a nonelected invention, the inventions must be amended in compliance with 37 C.F.R. 1.48(b) if one of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 C.F.R. 1.48(b) and by the fee required under 37 C.F.R. 1.17(i).

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Markush claims must be provided with support in the disclosure for each member of the Markush group. See MPEP 608.01(p). Applicant should exercise caution in making a selection of a single member for each substituent group on the base molecule to be consistent with the written description.

Rationale Establishing Patentable Distinctiveness Within Each Group

Each Group listed above is directed to or involves the use of compounds which are recognized in the art as being distinct from one another because of their diverse chemical structure, their different chemical properties, modes of action, different effects and reactive conditions (MPEP 806.04, MPEP 808.01). Additionally, the level of skill in the art is not such that one invention would be obvious over the other invention (Group), i.e. they are patentable over each other. Chemical structures, which are similar, are presumed to function similarly, whereas chemical structures that are not similar are not presumed to function similarly. The presumption even for similar chemical structures though is not irrebuttable, but may be overcome by scientific reasoning or evidence showing that the structure of the prior art would not have been expected to function as the structure of the claimed invention. Note that in accordance with the holding of Application of Papesch, 50 CCPA 1084, 315 F.2d 381, 137 USPQ 43 (CCPA 1963) and In re Lalu, 223 USPQ 1257 (Fed. Cir. 1984), chemical structures are patentably distinct where the structures are either not structurally similar, or the prior art fails to suggest a function of a claimed compound would have been expected from a similar structure.

The above groups represent general areas wherein the inventions are independent and distinct, each from the other because of the following reasons:

Inventions I and II are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be

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used to make other and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case, the products as claimed in Group I can be prepared by different processes as shown in Scheme M (page 58, line 18) and Scheme O (page 63, line 6) of the specification.

In addition, because of the plethora of classes and subclasses in each of the Inventions, a serious burden is imposed on the examiner to perform a complete search of the defined areas.

Therefore, because of the reasons given above, the restriction set forth is proper and not to restrict would impose a serious burden in the examination of this application.

Advisory of Rejoinder

The following is a recitation of M.P.E.P. 821.04, Rejoinder:

Where product and process claims drawn to independent and distinct inventions are presented in the same application, applicant may be called upon under 35 U.S.C. 121 to elect claims to either the product or process. See MPEP § 806.05(f) and § 806.05(h). The claims to the nonelected invention will be withdrawn from further consideration under 37 CFR 1.142. See MPEP § 809.02(c) and § 821 through § 821.03. However, if applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims, which depend from or otherwise include all the limitations of the allowable product claim will be rejoined.

Where the application as originally filed discloses the product and the process for making and/or using the product, and only claims directed to the product are presented for examination, when a product claim is found allowable, applicant may present claims directed to the process of making and/or using the patentable product by way of amendment pursuant to 37 CFR 1.121. In view of the rejoinder procedure, and in order to expedite prosecution, applicants are encouraged to present such process claims, preferably as dependent claims, in the application at an early stage of prosecution. Process claims, which depend from or otherwise include all the limitations of the patentable product will be entered as a matter of right if the amendment is presented prior to final rejection or allowance. Amendments submitted after final rejection are governed by 37 CFR 1.116. Process claims which do not depend from or otherwise include the limitations of the patentable product will be withdrawn from consideration, via an election by original presentation (see MPEP § 821.03). Amendments submitted after allowance are governed by 37 CFR 1.312. Process claims which depend from or otherwise include all the limitations of an allowed product claim and which meet the requirements of 35 U.S.C. 101, 102, 103, and 112 may be entered.

Where product and process claims are presented in a single application and that application qualifies under the transitional restriction practice pursuant to 37 CFR 1.129(b), applicant may either: (A) elect the invention to be searched and examined and pay the fee set forth in 37 CFR 1.17(s) and have the additional inventions searched and examined under 37 CFR 1.129(b)(2); or (B) elect the invention to be searched and examined and not pay the additional fee (37 CFR 1.129(b)(3)). Where no additional fee is paid, if the elected invention is directed to the product and the claims directed to the product are subsequently found patentable, process claims which either depend from or include all the limitations of the allowable product will be rejoined. If applicant chooses to pay the fees to have the additional inventions searched and examined pursuant to 37 CFR 1.129(b)(2) even if the product is found allowable, applicant would not be entitled to a refund of the fees paid under 37 CFR 1.129(b) by arguing that the process claims could have been rejoined. 37 CFR 1.26(a) states that "[T]he Commissioner may refund any fee paid by

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mistake or in excess of that required. A change of purpose after the payment of a fee...will not entitle a party to a refund of such fee..." In this case, the fees paid under 37 CFR 1.129(b) were not paid by mistake nor paid in excess, therefore, applicant would not be entitled to a refund. In the event of rejoinder, the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101,102, 103, and 112. If the application containing the rejoined claims is not in condition for allowance, the subsequent Office action may be made final, or, if the application was already under final rejection, the next Office action may be an advisory action. Form paragraphs 8.42 through 8.44 should be used to notify applicant of the rejoinder of process claims which depend from or otherwise include all the limitations of an allowable product claim.

In the event of rejoinder, the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104 - 1.106. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. If the application containing the rejoined claims is not in condition for allowance, the subsequent Office action may be made final, or, if the application was already under final rejection, the next Office action may be an advisory action.

The following is a recitation from paragraph five, "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. §103(b)" (1184 TMOG 86(March 26, 1996)):

"However, in the case of an elected product claim, rejoinder will be permitted when a product claim is found allowable and the withdrawn process claim depends from or otherwise includes all the limitations of an allowed product claim. Withdrawn process claims not commensurate in scope with an allowed product claim will not be rejoined." (emphasis added)

Therefore, in accordance with M.P.E.P. 821.04 and In re Ochiai, 71 F.3d 1565, 37 USPQ 1127 (Fed. Cir. 1995), rejoinder of product claims with process claims commensurate in scope with the allowed product claims will occur following a finding that the product claims are allowable. Until, such time, a restriction between product claims and process claims is deemed proper. Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution to maintain either dependency on the product claims or to otherwise include the limitations of the product claims. Failure to do so may result in a loss of the right to rejoinder.

During a telephone conversation with Ms. Wendy Hsu, Esquire on October 28, 2004 a provisional election was made *without traverse* to prosecute the invention of Group I, comprising

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Claims 1-6 of Formula II depicted in claim 2, page 164, line 2,

Further, an election of species was made of the compound depicted in claim 5, page 175, line 7,

Status of the Claims

Claims 1-9 are pending in this application. Claims 1-6 (in part) and 7-9 are withdrawn from further consideration by the examiner, 37 C.F.R. §1.142(b), as being drawn to a non-elected invention. The withdrawn subject matter is patentably distinct from the elected subject matter as it differs in structure and element and would require separate search considerations. In addition, a reference, which anticipates one group, would not render obvious the other.

The scope of the invention of the elected subject matter is as follows:

Compounds of formula, (n) , depicted in claim 2, wherein: R₄ is C2-C14 alkyl, C3-C10cycloalkyl, or aryl, R₅ is hydroxyl, halo, C1-C14 alkyl, C1-C14 alkoxyl,

acyl, R₅ and R₅ are hydrogen, hydroxyl, halo, C1-14 alkyl, C1-14 alkoxyl, acyl, R₆ is R₇ is hydrogen, hydroxyl, halo, C1-C14 alkyl, C1-14 alkoxyl, acyl; and R₉ is hydrogen, C1-C9 alkyl, C2-C9 alkenyl, 2-9 membered heteroalkenyl, C1C9 alkylamide, C1-C9 alkylcarboxamide, C1-C4 alkyl-cycloalkyl, C1-C4 alkyl-aryl, C3-C10 cycloalkyl, and aryl.

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As a result of the election and the corresponding scope of the invention identified supra, the remaining subject matter of claims 1-6 (in part) are withdrawn from further consideration pursuant to 37 CRF 1.142(b) as being drawn to non-elected inventions. The withdrawn compounds contain varying core structures, such as pyrimidinyl, piperidinyl, imidazolyl, pyrrolidinyl, etc., which are chemically recognized to differ in structure and function. This recognized chemical diversity of the functional groups can be seen by the various classifications of these functional groups in the U.S. Classification System. For instance, thiazoles are in various subclasses of class 548 and the heteroaryl moieties are in various subclasses of classes 544 (pyrimidines), 546 (pyridines), 548 (indoles), and 549 (thiophenes). Therefore the subject matter which are withdrawn from consideration as being non-elected subject matter differ materially in structure and composition and have been restricted properly.

Claims 1-6 (in part) and 7-9 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

⁽a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

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The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

- 1. Determining the scope and contents of the prior art.
- 2. Ascertaining the differences between the prior art and the claims at issue.
- 3. Resolving the level of ordinary skill in the pertinent art.
- 4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-6 (in part) are rejected under 35 U.S.C. 103(a) as being unpatentable over Chu et al., U.S. Pat. No. 6,720,346 in view of Chong et al., U.S. Pat. No. 6,569,878.

Applicants instant elected invention teaches the compound of formula,

dip depicted in claim 5, their multimers, pharmaceutically acceptable

salts, prodrugs, and active metabolites, wherein: R₄ is phenyl, R₅ is CH₃, R₅, and R₅, are F, R₆ is

$$R_9$$
, R_7 is hydrogen; and R_{9} is R_7 , yielding the compound depicted in claim 5,

page 175, line 7, or 4-[[4-amino-5-(2,6-difluoro-4-methyl-benzoyl)-2-thiazolyl]amino]-N-2-(1-methylethoxy)ethyl –benzenesulfonamide. These products, according to claims 8 and 9, page 176, lines 1-8, can be used for treating cellular proliferative diseases, cancer, autoimmune disease, viral disease, fungal disease, neurodegenerative disorder or cardiovascular disease.

Determination of the scope and content of the prior art (MPEP § 2141.01)

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Chu teaches thiazole benzamide compounds of formula,

thiazolyl]amino]-N-[2-(1-methylethoxy)ethyl]-benzamide, CAS RN 486413-88-1, and the pharmaceutically acceptable salt. (See US 6,720,346, Column 127, Example A7). These products can be used for the treatment of cellular proliferative diseases, cancer, autoimmune disease, viral disease, fungal disease, neurodegenerative disorder or cardiovascular disease (Column 1, lines 22-24). Chong discloses diamino substituted thiazole compounds and the pharmaceutically acceptable salts thereof depicted by the formula,

MeNH
$$=$$
 0
NH $=$

thiazolyl]amino]-N-methyl-benzenesulfonamide, CAS RN 223784-99-4. (See Pat. No. 6,569,878, Column 89, Example C (108)). These products can be used to alleviate the symptoms of cellular proliferative diseases and cancer (Column 3, lines 29-43).

Ascertainment of the difference between the prior art and the claims (MPEP § 2141.02)

The difference between the prior art of Chu and the claims is that in the instant application there is a benzenesulfonamide instead of a benzamide and a methyl group at the 4 position of the benzoyl group.

The difference between the prior art of Chong and the instantly claimed compounds is a methyl group attached to the sulfonamide and no substitution at the 4 position of the benzoyl group. In the instantly claimed application there is a methyl group at the 4 position of the benzoyl group and a methylethoxy-ethyl group attached to the sulfonamide while in Chong it is only a methyl group.

Finding of prima facie obviousness – rationale and motivation (MPEP § 2142-2413)

However, in the absence of showing unobvious results, it would have been obvious to one of ordinary skill in the art at the time of the invention when faced with Chu et al. and Chong et al. to make products that are useful for the treatment of cellular proliferative diseases and cancer, wherein 4-[[4-amino-5-(2,6-difluorobenzoyl)-2-thiazolyl]amino]-N-methylbenzenesulfonamide and 4-[[4-amino-5-(2,6-difluorobenzoyl)-2-thiazolyl]amino]-N-[2-(1-methylethoxy)ethyl]-benzamide is 4-[[4-amino-5-(2,6-difluoro-4-methyl-benzoyl)-2-thiazolyl]amino]-N-2-(1-methylethoxy)ethyl]-benzenesulfonamide.

Guided by the teaching of Chu and especially when faced with structurally related compounds of the secondary reference Chong one skilled in the art would be able to make similar compounds by replacing the carbonyl group in Chu with a sulphonyl group as taught in Chong. In addition, one skilled in the art would be able to make similar compounds by replacing the methyl group in Chong with a 2-(1-methylethoxy)ethyl group as taught in Chu. The motivation would be to prepare similar compounds pharmacologically active against cellular proliferative diseases and cancer.

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Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-8 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claims.

The specification failed to define the terms "metabolite" and "prodrug" so as to determine the structure of the compounds that are included and/or excluded by these terms.

"Metabolite" is understood to include "any product or substrate of metabolism, especially of catabolism, the breaking down in the body of complex chemical compounds into simpler ones," (Stedman's Medical Dictionary 27th Edition) but it is unclear what other elements are included by the term. Merely identifying a substance as a "metabolite" is insufficient to provide an enabling disclosure. Therefore, claims 1-8 are rejected. Applicant may overcome this rejection by defining the term "metabolite" in the specification.

"Prodrug" (as defined in the specification on page 22, lines 27-31) is indefinite. The definition provided is "a compound that may be converted under physiological conditions or by solvolysis to the specified compound or to a pharmaceutically acceptable salt of such compound" and that it "may be identified using routine techniques known in the art." This definition does not provide a clear description of what a "prodrug" is for this invention.

A proper definition of "prodrug" will address more than how the compounds were converted. The definition should also address the following exemplary list:

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-How were the prodrugs prepared? Ex. Prepared by modifying one of the functional groups. Then list the relevant functional groups.

- -What compounds are included in the definition of prodrug? Ex. Prodrugs include compounds of Formula I wherein a hydroxyl group is bonded to any group that may be cleaved in vivo to regenerate the free hydroxyl group respectively.
- -How are the prodrugs be metabolized? Ex. Prodrug can be metabolized before absorption.
- -How are the prodrugs utilized? Ex. Prodrug may be utilized to improve bioavailability.
- -What references were used? List the references.

Applicant can overcome this rejection by revising the definitions in the specification. However, applicants should note that the introduction of new subject matter into the specification will raise the issue of new matter. Alternatively, applicant is invited to point out where the definitions are in the original specification, claims or drawings.

Conclusion

Claims 1-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chu et al., U.S. Pat. No. 6,720,346 in view of Chong et al., U.S. Pat. No. 6,569,878 at this point in the examination process.

Telephone Inquiry

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susannah Lee whose telephone number is (571) 272-6098. The examiner can normally be reached on M-F, 8am-5pm.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on (571) 272-0699. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Susannah Lee Patent Examiner, AU 1626 Joseph K. McKane

Supervisory Patent Examiner

AU 1626

Date: 11/24/04